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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,206	09/14/2006	Irina Velikyan	PZ0333	6320

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,206	VELIKYAN ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 19 provides for the use of a kit, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

3. Claim 19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "strong anion exchanger" is a relative term. It is unclear as to what strong anion exchanger is preferred or would be acceptable for use with the present invention.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397A2) in view of Yngve (Dissertation **2001**) in further view of Maier-Borst et al. (GB 2056471A).

7. Griffiths et al. (WO03/059397A2) discloses the method of producing a ^{68}Ga-radiolabeled complex/^{68}Ga-labeled targeting agent for use in PET detection (p4, paragraph 2; p9, paragraph 1). The method of obtaining the ^{68}Ga involves eluting ^{68}Ga from a ^{68}Ge/^{68}Ga titanium dioxide based in-house generator. The ^{68}Ga is eluted from the titanium dioxide generator, which can be fitted with an anion-exchange membrane/Q5F cartridge (p14, paragraph 1) with acidic solution, such as 0.5-1N HCl (p7, paragraph 3; p8, paragraph 2; p12, paragraph 1). The method of producing a radiolabeled gallium complex involves reacting the solution of a peptide labeled macrocyclic chelate with the ^{68}Ga diluted from the ^{68}Ge/^{68}Ga titanium dioxide generator (p14, paragraph 1). The chelate-targeting agent conjugates can be compounded into kits that are ready to use and accept the ^{68}Ga elute (p8, paragraph 3). The macrocyclic-chelating agent, such as DOTA or NOTA may be linked to a peptide that can target the site of a disease, thus generating a bifunctional chelating agent comprising a targeting vector which will be site-specific (p9, paragraph 1; p11, paragraphs 1 and 2). Griffiths et al. does not disclose the preparation of the chelate-targeting agent conjugates via microwave acceleration. Griffiths et al. also does not disclose an anion exchanger comprising HCO_3^- or more specifically one comprising a amine functional groups or one based on polystyrene-divinylbenzene.

8. Yngve (Dissertation **2001**) discloses the method of obtaining ^{68}Ga from a $^{68}Ge/^{68}Ga$ generator attached to an ion-exchange column which is eluted with 0.1M HCl (p39, paragraph 3). The preparation of a phosphorothiolated ^{68}Ga-DOTA-oligonucleotide and a ^{68}Ga-DOTA-octreotide is also disclosed and that the protocol for labeling such DOTA macromolecules is suitable for kit type preparations (abstract; p39, paragraph 4; p41; p49, paragraph 2). The abstract also discloses the use of microwave technology for the preparation of other compounds, such as ^{76}Br-labeled octreotide derivatives (abstract; p36, paragraph 2).

9. Maier-Borst et al. (GB 2056471A) discloses the separation of ^{68}Ga for its parent nuclide with water via passing the eluant from a generator column into an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and washing the anion exchanger with water (p4, lines 44-48).

10. At the time of the invention it would have been obvious to produce a ^{68}Ga-DOTA-oligonucleotide complex (see disclosures above) for use as a PET tracer via the production of ^{68}Ga from a $^{68}Ge/^{68}Ga$ titanium dioxide generator as disclosed by Griffiths et al. The microwave synthesis technique for the method of producing labeled complexes was known by Yngve thus, it would have been obvious to utilize the microwave acceleration technique for a faster, more reproducible preparation of the ^{68}Ga-DOTA-oligonucleotide complex that generates minimal side products. Microwave acceleration techniques have been utilized since the 1980's in a number of production methods for radioactive precursors and radiotracers labeled with positron-emitting nuclides. The microwave method is mostly associated with shortened reaction times

and encompasses the microwave conditions of the instant claims. Since the microwave technique was utilized by Yngve (Int. Diss. Abs. **2001**, *62,* abstract) it would have been obvious to try all radiotracer-labeling reactions with the microwave technique.

11. It would have been obvious to utilize an anion exchanger of Maier-Borst et al. to separate ^{68}Ga from its parent nuclide since no chelating agent is required for separation. It is known in the art to add a chelating agent, such as EDTA to elute ^{68}Ga from an aluminum oxide exchanger. The disadvantage of forming the ^{68}Ga-EDTA complex is that the complex has to be destroyed before further processing to obtain radiopharmaceutical agents which is time-consuming and expensive (see Maier-Borst et al. p1, lines 10-16).

12. Claims 1,3-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Velikyan et al. (*J. Labelled Comp. Radiopharm.* **2004**, *47*, 79-89/published online 12/29/03) in view of Maier-Borst et al. (GB 2056471A).

13. Velikyan et al. (*J. Labelled Comp. Radiopharm.* **2004**, *47*, 79-89/published online 12/29/03) discloses the method of obtaining ^{68}Ga from a generator column and contacting the eluate from the generator column with an ion-exchange column in 0.1MHCl (p86, paragraph 2). The method of labeling synthesis of radiolabeled gallium complex to produce an oligonucleotide (targeting vector) bound ^{68}Ga-DOTA via microwave (1 min at 100W) accelerated complexation is also disclosed (p80, paragraph 3; p83, paragraph 1; p82, scheme 1). The ^{68}Ga was eluted and collected from the ^{68}Ge ion-exchange column and reacted with the DOTA-oligonucleotide in the microwave for 1

min at 100W to generate the radiolabeled gallium complex ^{68}Ga-DOTA-oligonucleotide (p83, paragraph 1; p86). ^{68}Ga is a good candidate for labeling of oligonucleotides since it forms stable complexes with non- and macrocyclic bifunctional chelators containing nitrogen and oxygen donors (p80, paragraph 2). The radiolabeled gallium complex ^{68}Ga-DOTA-oligonucleotide can be used for PET and can be prepared from kits (p80, paragraph 1). Velikyan et al. does not disclose an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene.

14. Maier-Borst et al. (GB 2056471A) discloses the separation of ^{68}Ga for its parent nuclide with water via passing the eluant from a generator column into an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and washing the anion exchanger with water (p4, lines 44-48).

15. At the time of the invention t would have been obvious to one ordinarily skilled in the art to utilize an anion exchanger of Maier-Borst et al. to separate ^{68}Ga from its parent nuclide since no chelating agent is required for separation. It is known in the art to add a chelating agent, such as EDTA to elute ^{68}Ga from an aluminum oxide exchanger. The disadvantage of forming the ^{68}Ga-EDTA complex is that the complex has to be destroyed before further processing to obtain radiopharmaceutical agents which is time-consuming and expensive (see Maier-Borst et al. p1, lines 10-16).

Double Patenting

16. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to

identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

17. Claims 8-12 and 14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1,3-7,11,13,15 of copending Application No. 10/552,134. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1,2,6-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 11/358,681. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method for producing a ^{68}Ga-radiolabelled complex of the instant claims encompasses the method for labeling synthesis of radiolabeled gallium complex of 11/358,681. The method of the instant claims includes the method of obtaining ^{68}Ga by contacting the eluate from a ^{68}Ge/^{68}Ga generator which is also disclosed in the method of 11/358,681. The macrocyclic chelating agents (DOTA), the generator column (titanium dioxide), the strong anion exchangers and the use of microwave activation for the preparation are identical for the instant claims and copending Application No. 11/358,681. The species of targeting vector protein, such as hEGF of 11/358,681 anticipate the genus of targeting vector proteins of the instant claims. Therefore, the resulting radiolabeled gallium complex of the instant claims is obviously generated and isolated via the synthesis and would encompass that radiolabeled gallium complex of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/552,134. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of producing a

^{68}Ga-radiolabeled complex of the instant claims encompasses the method of producing a radiolabeled gallium complex of the copending Application No. 10/552,134 since the method steps are identical. Both inventions involve reacting a ^{68}Ga radioisotope with a macrocyclic or bifunctional chelating agent via microwave. The inventions also include a targeting moiety that may be bound to the chelating agent for site-directed localization. The generation of the ^{68}Ga radioisotope of both applications involves eluting the ^{68}Ga from a ^{68}Ge/^{68}Ga titanium dioxide generator followed by purification of the ^{68}Ga eluate via a strong anion exchanger. Therefore, the resulting radiolabeled gallium complex of the instant claims is obviously generated via the synthesis and isolated and would encompass that radiolabeled gallium complex of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
February 27, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER